REMARKS/ARGUMENTS

Claims 1-15 and 17-65 are pending in the above-referenced patent application; claims 1-3, 5-11, 18, 24, 25, 36-38, 44, 46, 49, 61 and 63 are currently under examination. As suggested by the Examiner in the Office Action, claim 1 has been amended to delete the proviso "if R^1 is $-N(CH_3)_2$, R^2 is hydroxy, R^4 is alkyl and X is =O, then R^3 is other than hydroxyl." In addition, claim 1 has been amended to claim the subject matter of the present invention with greater particularity. More specifically, the remaining proviso set forth in claim 1 has been amended to recite that "if R^1 is $-C(O)CH_3$, $-OCH_3$, $-SCH_3$, $-N(CH_3)_2$ or $-NHCH_3$, R^2 is hydrogen, R^3 is acetyloxy and R^4 is methyl, then X is other than =O and $=N-OR^5$, wherein R^5 is methyl." No new matter has been introduced by the present amendments to claim 1 and, thus, Applicants respectfully request entry of such amendments.

Applicants express their gratitude to the Examiner for withdrawing the 35 U.S.C. § 102(b) rejection over Cook *et al.* (U.S. Patent No. 5,073,548).

Reconsideration of the application is respectfully requested in view of the above amendment to claim 1 and the following remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

I. Provisional Obviousness-Type Double Patenting Rejection

The Examiner has provisionally rejected claims 1-3, 5-8, 9, 24, 25, 36-38, 46, 49, 61 and 63 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-26 of copending U.S. Patent Application No. 09/180,132.

As noted by the Examiner in the Office Action, upon notification that allowable subject matter is present in the instant application, Applicants will file the appropriate Terminal Disclaimer under 37 CFR § 1.321(c) to overcome the rejection.

II. Rejection Under 35 U.S.C. § 112, Second Paragraph

In the Office Action, claims 1-3, 5 and 7-9 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for reciting a proviso that does not have proper antecedent basis in the claim. The Examiner has indicated in the Office Action that this rejection can be overcome by deleting the proviso from claim 1 (*see*, page 3 of the Office Action).

In accordance with the Examiner's suggestion and in order to expedite prosecution, Applicants have amended claim 1 to delete the proviso "if R^1 is $-N(CH_3)_2$, R^2 is hydroxy, R^4 is alkyl and X is =O, then R^3 is other than hydroxyl." In view of this amendment to claim 1, the Examiner's rejection is rendered moot. Accordingly, Applicants urge the Examiner to withdraw this rejection.

III. Rejection Under 35 U.S.C. § 103 Over Cook et al.

In the Office Action, claims 1-3, 6-11 and 49 have been rejected under 35 U.S.C. § 103 as allegedly obvious over Cook *et al.* (U.S. Patent No. 5,073,548). In making this rejection, the Office Action states that Cook *et al.* disclose a genus of 17β-acetyl substituted compounds having anti-progestational and/or antiglucocorticoid properties and cites to the specification and, in particular, Compound 8a in Table 2 in support of this position.

Applicants respectfully submit that claim 1 has previously been amended to remove Compound 8a of Cook *et al.* from the scope of claim 1. In addition, claim 1 has currently been amended to delete the compounds wherein R^1 is $-N(CH_3)_2$, $-OCH_3$ or $-SCH_3$, R^2 is hydrogen, R^3 is acetyloxy, R^4 is methyl and X is $=N-OR^5$, wherein R^5 is methyl, which are not specifically taught or suggest by Cook *et al.*, but which hypothetically fall within the scope of the compounds of Structure A disclosed in the specification of Cook *et al.*

Applicants respectfully submit that Cook *et al.* does not teach or suggest the compounds of amended claim 1. In fact, a perusal of the other compounds of Cook *et al.* reveals that Cook *et al.* only specifically discloses compounds of Structure A, wherein R^1 (which corresponds to R^3 of the presently claimed compounds) is H, C_{1-4} alkyl, C_{2-4} alkenyl and C_{2-4} alkynyl. Moreover, Cook *et al.* explicitly state that "[a]dditional preferred compounds are those

in which. . . R^1 is acetoxy or C_{2-6} alkynyl groups" (*see*, column 4, lines 26-28 of Cook *et al.*). As the Examiner is aware, such compounds of Cook *et al.* do ***not*** fall within the scope of amended claim 1. More importantly, such compounds of Cook *et al.* do ***not*** teach or suggest the compounds of claim 1. Absent such a teaching or suggestion, the presently claimed compounds are nonobvious and, thus, patentable over Cook *et al.* Accordingly, Applicants urge the Examiner to withdraw the rejection under 35 U.S.C. § 103 over Cook *et al.*

IV. Rejection Under 35 U.S.C. § 103 Over Cook et al. in view of Peeters et al.

In the Office Action, claims 1-3, 5-11, 18, 24, 25, 44, 46, 61 and 63 under 35 U.S.C. § 103 as allegedly obvious over Cook *et al.* (U.S. Patent No. 5,073,548) in view of Peeters (U.S. Patent No. 5,741,787). Cook *et al.* is cited for the reasons set forth above. In addition, Peeters is cited as disclosing "a generic group of steroids that encompass the compounds taught by Cook having antiglucocorticoid properties useful for treatment of anxiety disorders" (*see*, page 5 of the Office Action).

For the reasons set forth above, Cook *et al.* do not teach or suggest the compounds of claim 1. Moreover, Peeters does ***not*** supply the teaching, suggestion or motivation to combine that is missing from Cook *et al.* More particularly, as explained by Dr. Kim in his declaration, which was filed in the USPTO on August 14, 2002 pursuant to 37 C.F.R. § 1.132, the compounds that Peeters exemplifies and enables ***differ*** from the present invention in the stereochemistry at C-17. Except for a single *intermediate*, the compounds described in Peeters all have a hydroxyl group as R5 on the Peeters generic, *i.e.*, a β-hydroxy substituent. That intermediate (*see*, Example 5(b)-(c) in Peeters, at column 7, lines 56-62) lacks a second substituent at C-17, and further lacks the C-3 carbonyl of the present invention. The carbonyl on the A-ring in that compound is also protected as a dioxolane acetal; thus, according to Dr. Kim, that intermediate is ***not*** analogous to the claimed compounds of the present invention. As set forth by Dr. Kim, in every compound described in Peeters that contains both a hydroxyl and another substituent at C-17, the hydroxyl is β, *i.e.*, it is the R5 substituent, whereas the β substituent in the present invention is necessarily an acyl group, and a hydroxyl or other group in

the claimed compounds can only be α. Clearly, the compounds exemplified by Peeters have the ***opposite*** (or inverted) stereochemistry at C-17 from the claimed compounds.

Moreover, as pointed out by Dr. Kim in his declaration, the scope of the examples in Peeters is extremely narrow: the overall teaching offers very limited direction to one motivated to synthesize antiglucocorticoid compounds substantially different from the few described. The ***six*** novel compounds named and tested are all 17-β-hydroxy-17-α-alkynes. It is not apparent, in Dr. Kim's opinion, that one of skill in the art would foresee a "reasonable expectation of success" from such limited precedent in the synthesis of compounds where (a) the stereochemistry at C-17 is inverted, (b) an sp^2 carbon substituent is incorporated at C-17 in place of the sp-hybridized carbon of the alkyne group, and (c) a heteroatom (the carbonyl oxygen of the acyl group in the present invention) is introduced at the R5 substituent, ***simultaneously*** changing three features that were conserved in ***each*** of the compounds shown to possess the activity of interest in Peeters.

Further, it is Dr. Kim's opinion that Peeters does not provide motivation to synthesize the compounds of the present invention. Peeters' preferred embodiments specify "R_4 is prop-1-ynyl, R_5 is hydroxy" (*see*, Peeters, column 2 at line 53), which gives the opposite stereochemistry at C-17 from compounds that would be analogous to the compounds of the present invention. Other than including a generalized acyl group in a list of substituents that *could* be used for R5, and similarly including hydroxy in an array of substituents to be considered for R4, it gives no indication which substituents stand out aside from that preferred embodiment description. Since the preferred compounds have the opposite (or inverted) stereochemistry from compounds analogous to those of the present invention, what little direction Peeters does provide ***teaches away*** from analogs that would render the present invention obvious, in Dr. Kim's opinion, by teaching that the activity is associated with the opposite stereochemistry at C-17.

As pointed out by Dr. Kim, Tables 1 and 2 of the present application provide activity data showing the relative antiglucocorticoid and antiprogestational activities of selected compounds. In Dr. Kim's opinion, this data is surprising because it demonstrates that the

antiglucocorticoid activity can be substantially separated from antiprogestational activity with the compounds of the present invention. In Peeters, the compounds possess very substantial antiglucocorticoid activity. In contrast, the compounds of the present invention possess antiprogestational activity, with substantially less antiglucocorticoid activity. In Dr. Kim's opinion, this is a highly significant separation of properties, because the reduced antiglucocorticoid activity greatly enhances the clinical potential for extended therapeutic applications.

Furthermore, as explained by Dr. Kim, Peeters only provides one synthesis route to create the stereochemistry at C-17 (*see*, Example 5(d), column 8 at lines 7-21 of the Peeters patent). This synthesis route involves the addition of acetylene to a ketone at C-17 and, based on the yields reported, it produces ***quantitatively*** the *beta*-hydroxy product. According to Dr. Kim's calculations, which are set forth in his declaration, there is no indication that the other isomer, which *might* be useful to prepare compounds of the present invention, was produced, and no other method to create a chiral tertiary alcohol center at C-17 is taught. All other examples in Peeters directed to the synthesis of compounds with a carbon-based substituent at C-17 begin with the *beta*-hydroxy in the R5 position of the Peeters generic compound. Some involve modification of the acetylenic group, but in Dr. Kim's opinion, none provides a way to invert that center or to introduce an acyl substituent at C-17.

In fact, as explained by Dr. Kim in his declaration, their attempts to functionalize an acyl group at C-17 in the presence of the 11-β-dimethylaminophenyl group, which is a preferred substituent in the compounds of the present invention, demethylation of the dimethylamino group rather than the desired functionalization of the acyl group was observed. This finding has been published by Dr. Kim in *J. Chem. Soc. Chem. Commun.*1985-86 (1994), a copy of which is attached to his declaration as Exhibit B. According to Dr. Kim, preparation of the claimed compounds required that a new synthetic route be developed. As such, according to Dr. Kim, Peeters does not enable the synthesis of compounds of the present invention by one of ordinary skill in the art.

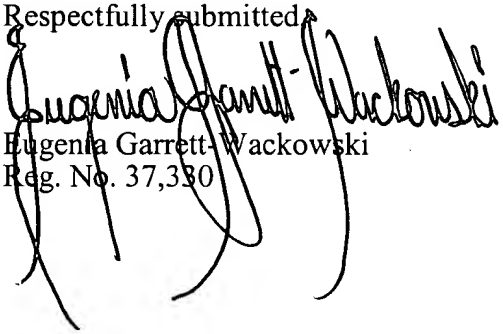
In view of the foregoing remarks and the previously filed declaration of Dr. Kim, claims 1, 2, 4-7, 15-19, 26 and 27 are non-obvious and, thus, patentable over Cook *et al.* in view of Peeters. Accordingly, Applicants urge the Examiner to withdraw the obviousness rejection under 35 U.S.C. § 103 over Cook *et al* in view of Peeters.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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